

Summary of Carcinogenic Potency and Positivity for 492 Rodent Carcinogens in the Carcinogenic Potency Database

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A tabulation of carcinogenic potency (TD₅₀) by species for 492 chemicals that induce tumors in rats or mice is presented. With the use of the Carcinogenic Potency Database, experimental results are summarized by indicating in which sex-species groups the chemical was tested and the respective evaluations of carcinogenicity. A comparison of three summary measures of TD₅₀ for chemicals with more than one positive experiment per species shows that the most potent TD₅₀ value is similar to measures that average values or functions of values. This tabulation can be used to investigate associations between rodent potency and other factors such as mutagenicity, teratogenicity, chemical structure, and human exposure.

Introduction

For a variety of purposes it is desirable to have a summary measure of the carcinogenic potency of a chemical in rodents. A single value is needed, for example, to summarize the chronic toxicity of a chemical, to estimate carcinogenic hazards to humans by a comparison of rodent potency and human exposure (1,2), or to compare results of short-term tests with those of rodent bioassays (3). For several years we have been developing the Carcinogenic Potency Database (CPDB), a compilation of the results of chronic rodent cancer tests and the potency values derived from those results (4-6). The CPDB contains data on approximately 3700 experiments of 975 compounds, including tests from the National Cancer Institute and National Toxicology Program (NCI/NTP), as well as from the general published literature. For a given compound, the database may include experiments in both rats and mice, males and females, a variety of strains or routes of administration, and a variety of doses and experimental conditions; alternatively, for a different substance there may be only one experiment conducted in a single sex-species group. In order to construct a chemical-by-chemical list of carcinogenic potency in each species, some

method must be selected to summarize the potency of a carcinogen when there is more than one potency estimate for it. Additional information to summarize the experimental results includes the number of sex-species groups tested and the evaluations of carcinogenicity in each group.

In this paper we present a table summarizing carcinogenic potency in rats and mice for the 492 chemicals that have positive results in the CPDB; we also indicate in which sex-species groups the chemical was tested and the respective evaluations of carcinogenicity. Our intent is that this summary compilation will be a useful reference source for the scientific and regulatory communities, and that it will facilitate the use of our larger published plots of the CPDB. The larger plots provide detailed information on each experiment including the species, sex, strain, route of administration, duration of exposure and of experiment, dose levels, target sites, shape of the dose response, estimates of carcinogenic potency and the confidence limits surrounding it, statistical significance of the carcinogenic dose response, tumor incidences, and bibliographic citation to the published paper or to the NCI/NTP Technical Report.

Methods

Our analyses are based on the chemicals reported in the CPDB (4-6), which has been fully described in

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Gold et al. (4) as to bioassay inclusion criteria, protocol characteristics and derived variables. The database is organized by chemical using a plot format and includes bioassay results from two sources: papers published in the general literature through 1984, and NCI/NTP Technical Reports published through May 1986. All experiments in the database meet a specific set of inclusion criteria that were designed to permit the estimation of carcinogenic potency; therefore, reasonable consistency of experimental protocols is assured. Rodent bioassays are included in the database only if the test agent was administered alone rather than in combination with other substances; if the bioassay included a control group; if the route of administration was either diet, water, gavage, inhalation, IV injection or IP injection; and if the length of experiment in rodents was at least 1 year with dosing for at least 6 months. For the CPDB, we do not evaluate the evidence for carcinogenicity in an experiment; rather, we report the evaluation of the published author and calculate the statistical significance of the tumorigenic dose response in the experiment.

Carcinogenicity

Our tabular compilation of results by sex-species group and of carcinogenic potency by species is restricted to chemicals identified as carcinogens in our database. We classify the results of an experiment as either positive or negative on the basis of the author's opinion in the published paper, and we include in the present publication only those chemicals that have been evaluated as positive by the author of at least one experiment. In some cases authors do not clearly state their evaluation, and in some NCI/NTP Technical Reports the evidence for carcinogenicity is considered only suggestive; in our analyses we consider these cases as lacking clear evidence of carcinogenicity and do not use them to identify a chemical as positive. We use the author's opinion to determine positivity because it often takes into account more information than statistical significance alone, such as historical control rates for particular sites, survival and latency, and/or dose response. Generally, this designation by author's opinion corresponds well with the results of statistical tests for the significance of the dose-response effect (4,7).

In our tabular compilation of positivity by sex-species group for each of the 492 chemicals classified as positive, we indicate whether the compound was tested in each group and list the strongest level of evidence for carcinogenicity based upon any author's evaluation in either the general literature or the NCI/NTP. The strongest evaluation is clear evidence of carcinogenicity (+). When there was no such evaluation in one of the sex-species groups, but the compound was tested by NCI/NTP and their evaluation was stronger than "no evidence of carcinogenicity" (-), we indicate whether that NCI/NTP evaluation was "some evidence of carcinogenicity" (A), "equivocal" (E) or "in-

adequate bioassay" (I). These evaluations correspond to the opinions reported in our published plots; we note that in a few borderline cases our interpretation of the Technical Reports differs from those recently tabulated by Haseman et al. (8).

Carcinogenic Potency Values

In our analyses of carcinogenic potency we use our numerical index, the TD_{50} , which has been fully described in Sawyer et al. (9) and in Peto et al. (10), and which is reported for each target site in our published plots. Briefly, TD_{50} may be defined as follows: For a given target site(s), TD_{50} is the chronic dose rate in milligrams per kilogram body weight per day that would induce tumors in half the test animals at the end of a standard lifespan for the species in the absence of tumors in control animals. Since the tumor(s) of interest often occurs in control animals, TD_{50} is more precisely defined as the chronic dose rate that will halve the probability of remaining tumor-free throughout the standard lifespan of the species (9,10). For bioassays from the NCI/NTP program, TD_{50} values are estimated from lifetable data (11) and are adjusted for the differential effects of toxicity among dose groups and for differences in the time pattern of tumor incidence. For experiments from the general literature, TD_{50} values are based on summary incidence data [for a comparison of methods and TD_{50} values see (9,11)]. The range of TD_{50} values for carcinogens in the CPDB is more than 10 million-fold.

For the purposes of this summary, in any given positive experiment we select the lowest TD_{50} value from among positively evaluated target sites with a statistically significant dose response (two-tailed $p < 0.1$). If no positive sites have a significant dose response, then we select the most potent (lowest TD_{50}) from among positively evaluated sites with $p \geq 0.1$. This method provides a single TD_{50} to represent an experiment. For approximately one-half of the carcinogens in rats and one-third of the carcinogens in mice, the CPDB includes only one positive experiment. For chemicals with more than one positive test, we summarize potency in a species by selecting the lowest significant TD_{50} value from among those representing each experiment. If none is significant, the lowest is chosen from among these nonsignificant values. In some experiments, no TD_{50} could be estimated because all animals in the only dose group had the tumor of interest, and the only data available were for crude percentages of animals with a tumor (4). For these cases we use the 99% upper confidence limit of TD_{50} as a replacement for the TD_{50} .

Results

In Table 1 we report results for the 492 test agents that were evaluated by a published author as tumorigenic in at least one experiment. These are the 492 positive

Table 1. Carcinogenic potency in mg/kg/day (TD₅₀) and positivity in rats and mice for chemicals evaluated as carcinogens in at least one experiment.

Rat	Mouse	MR	FR	MM	FM	CAS	Name
NT	1.61 ^a	NT	NT	+	+	16568-02-8	ACETALDEHYDE METHYLFORMYLHYDRAZONE
104 ^a	3010	+	+	+	-	60-35-5	ACETAMIDE
-	1010 ^a	-	NT	+	+	103-90-2	ACETAMINOPHEN
6.05	NT	NT	+	NT	NT	18523-69-8	ACETONE[4-(5-NITRO-2-FURYL)-2-THIAZOLYL]HYDRAZONE
12.1	NT	+	-	NT	NT	127-06-0	ACETOXIME
21.1 ^a	-	+	NT	-	NT	34627-78-6	1'-ACETOXYSAFROLE
NT	208 ^a	NT	NT	+	+	65734-38-5	N'-ACETYL-4-(HYDROXYMETHYL)PHENYLHYDRAZINE
NT	319 ^a	NT	NT	+	+	1078-38-2	1-ACETYL-2-ISONICOTINOYLHYDRAZINE
NT	44.8 ^a	NT	NT	+	+	114-83-0	1-ACETYL-2-PHENYLHYDRAZINE
1.18	NT	NT	+	NT	NT	4075-79-0	4-ACETYLAMINOBIIPHENYL
0.841 ^a	4.78 ^{af}	+	+	+	+	53-96-3	2-ACETYLAMINOFLUORENE
0.395 ^a	NT	+	+	I	I	7008-42-6	ACRONYCINE
5.31 ^{af}	NT	+	+	NT	NT	107-13-1	ACRYLONITRILE
7.69E-4 ^{ad}	NT	+	+	NT	NT	50-76-0	ACTINOMYCIN D
11.4 ^{af}	72.9 ^{af}	+	+	+	+	3688-53-7	AF-2
0.00247	NT	+	NT	NT	NT	29611-03-8	AFLATOXICOL
9.32E-4 ^{af}	-	+	+	-	-	1162-65-8	AFLATOXIN B1
0.00187 ^a	0.343	+	NT	+	NT	---	AFLATOXIN, CRUDE
-	0.741 ^a	-	-	+	B+	309-00-2	ALDRIN
96	-	+	A	-	-	57-06-7	ALLYL ISOTHIOCYANATE
123	62.8	+	-	-	+	2835-39-4	ALLYL ISOVALERATE
NT	30.9 ^a	NT	NT	+	+	52207-83-7	ALLYLHYDRAZINE.HCl
NT	25 ^a	NT	NT	+	+	75104-43-7	3-AMINO-1,4-DIMETHYL-5H-PYRIDO 4,3-b INDOLE ACETATE
-	2070	-	-	+	-	17026-81-2	3-AMINO-4-ETHOXYACETANILIDE
11.8 ^a	30.5 ^a	+	+	+	+	mixture	3-AMINO-9-ETHYLCARBAZOLE MIXTURE
NT	15.6 ^a	NT	NT	+	+	68006-83-7	2-AMINO-3-METHYL-9H-PYRIDO- 2,3-b -INDOLE
5.32	6.81 ^{af}	-	+	+	+	72254-58-1	3-AMINO-1-METHYL-5H-PYRIDO 4,3-b INDOLE ACETATE
34.1 ^a	174	+	+	-	+	82-28-0	1-AMINO-2-METHYLANTHRAQUINONE
3.25 ^a	5.08 ^a	+	+	+	+	67730-11-4	2-AMINO-6-METHYLDIPYRIDO 1,2-a:3',2'-d IMIDAZOLE
NT	17.5 ^a	NT	NT	+	+	76180-96-6	2-AMINO-3-METHYLIMIDAZO 4,5-f QUINOLINE
3.67	NT	NT	+	NT	NT	3775-55-1	2-AMINO-5-(5-NITRO-2-FURYL)-1,3,4-OXADIAZOLE
0.662	NT	NT	+	NT	NT	712-68-5	2-AMINO-5-(5-NITRO-2-FURYL)-1,3,4-THIADIAZOLE
5.85	7.87	NT	+	NT	+	38514-71-5	2-AMINO-4-(5-NITRO-2-FURYL)THIAZOLE
NT	105 ^a	NT	NT	+	+	28754-68-9	trans-5-AMINO-3,2-(5-NITRO-2-FURYL)VINYLYL-1,2,4-OXADIAZOLE
309	-	+	A	-	-	119-34-6	4-AMINO-2-NITROPHENOL
NT	9.95	NT	NT	NT	+	2104-09-8	2-AMINO-4-(p-NITROPHENYL)THIAZOLE
44.6	-	A	+	-	-	121-66-4	2-AMINO-5-NITROTHIAZOLE
NT	35.6 ^a	NT	NT	+	+	26148-68-5	2-AMINO-9H-PYRIDO(2,3-b)INDOLE
101	755 ^a	+	-	+	+	117-79-3	2-AMINOANTHRAQUINONE
3.7 ^a	-	+	+	-	NT	97-56-3	o-AMINOAZOTOLUENE
NT	0.993 ^a	NT	NT	+	+	92-67-1	4-AMINODIPHENYL
NT	3.36 ^{ac}	NT	NT	+	+	3693-22-9	2-AMINODIPHENYLENE OXIDE
33.8 ^a	12 ^a	+	+	+	+	67730-10-3	2-AMINODIPYRIDO 1,2-a:3',2'-d IMIDAZOLE
8.75 ^a	24.5 ^a	+	+	+	+	61-82-5	3-AMINOTRIAZOLE
833	-	+	-	-	-	2432-99-7	11-AMINOUNDECANOIC ACID
0.532 ^a	NT	+	+	NT	NT	10589-74-9	1-AMYL-1-NITROUREA
88 ^{af}	-	+	+	-	-	142-04-1	ANILINE.HCl
27.8 ^a	935 ^a	+	+	+	+	134-29-2	o-ANISIDINE.HCl
61.8 ^a	158	B+	B+	+	-	140-57-8	ARAMITE
NT	33.6 ^a	NT	NT	+	+	61-94-9	ARECOLINE.HCl
-	9.58	A	A	+	NT	27323-18-8	AROCLOR 1254
1.04 ^a	NT	+	+	NT	NT	11096-82-5	AROCLOR 1260
11	39.2 ^a	+	NT	+	+	2465-27-2	AURAMINE-O
0.793 ^d	NT	B+	B+	NT	NT	115-02-6	AZASERINE
19.2 ^a	-	+	+	-	-	103-33-3	AZOBENZENE
0.0302	NT	+	NT	NT	NT	25843-45-2	AZOXYMETHANE
51.1 ^{af}	15.1 ^{af}	+	+	+	+	71-43-2	BENZENE
1.73	NT	B+	B+	NT	NT	92-87-5	BENZIDINE
NT	8.99 ^a	NT	NT	+	+	531-85-1	BENZIDINE.2HCl

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Table 1. (Continued)

Rat	Mouse	MR	FR	MM	FM	CAS	Name
0.956	11	B+	B+	+	-	50-32-8	BENZO(a)PYRENE
NT	7.35 ^a	NT	NT	+	+	613-94-5	BENZOYL HYDRAZINE
NT	85.3	NT	NT	-	+	20570-96-1	BENZYLHYDRAZINE.2HCl
-	1120	-	-	A	+	2185-92-4	2-BIPHENYLAMINE.HCl
-	138 ^a	-	-	+	+	108-60-1	BIS(2-CHLORO-1-METHYLETHYL) ETHER
NT	8.19 ^a	NT	NT	+	-	111-44-4	BIS-2-CHLOROETHYLETHYR
NT	4.62 ^d	NT	NT	NT	+	13483-18-6	BIS-1,2-(CHLOROMETHOXY)ETHANE
NT	3.11 ^d	NT	NT	NT	+	56894-91-8	BIS-1,4-(CHLOROMETHOXY)-p-XYLENE
0.00357	0.182 ^{ae}	+	NT	+	+	542-88-1	BIS-(CHLOROMETHYL) ETHER
3.14	NT	+	NT	NT	NT	---	4-BIS(2-HYDROXYETHYL)AMINO-2-(5-NITRO-2-THIENYL) QUINAZOLINE
NT	34.5 ^a	NT	NT	+	-	23746-34-1	BIS-2-HYDROXYETHYLDITHIOCARBAMIC ACID, POTASSIUM
0.945 ^a	NT	+	+	NT	NT	1937-37-7	C.I. DIRECT BLACK 38
-	208 ^a	E	A	+	+	2784-94-3	HC BLUE NO. 1
89.3 ^a	-	+	+	E	-	2475-45-8	C.I. DISPERSE BLUE 1
1.18 ^a	NT	+	+	NT	NT	2602-46-2	C.I. DIRECT BLUE 6
9.62 ^a	-	+	+	-	-	7758-01-2	BROMATE, POTASSIUM
2.07	NT	-	+	NT	NT	16071-86-6	C.I. DIRECT BROWN 95
NT	28.8 ^a	NT	NT	+	+	106-99-0	1,3-BUTADIENE
NT	19.2 ^a	NT	NT	+	+	---	N-N-BUTYL-N-FORMYLHYDRAZINE
0.432 ^a	NT	+	NT	NT	NT	3817-11-6	N-BUTYL-N-(4-HYDROXYBUTYL)NITROSAMINE
0.91 ^a	NT	+	+	NT	NT	869-01-2	N-N-BUTYL-N-NITROSOUREA
349 ^a	-	+	+	B-	B-	25013-16-5	BUTYLATED HYDROXYANISOLE
-	368	-	-	+	-	128-37-0	BUTYLATED HYDROXYTOLUENE
NT	38.1 ^a	NT	NT	+	+	---	1,1-DI-N-BUTYLHYDRAZINE
NT	9.03 ^a	NT	NT	+	+	56795-65-4	N-BUTYLHYDRAZINE.HCl
NT	34.5 ^a	NT	NT	+	+	7422-80-2	1,2-DI-N-BUTYLHYDRAZINE.2HCl
13.8	NT	NT	+	NT	NT	3068-88-0	beta-BUTYROLACTONE
NT	89.4 ^a	NT	NT	+	+	2425-06-1	CAPTAOL
NT	223 ^a	NT	NT	+	+	563-41-7	CARBAMYL HYDRAZINE.HCl
NT	155 ^a	NT	NT	+	+	103-03-7	1-CARBAMYL-2-PHENYLHYDRAZINE
14.1	-	B+	B+	-	-	63-25-2	CARBARYL
NT	102 ^a	NT	NT	+	+	86-74-8	CARBAZOLE
0.765 ^{abe}	114 ^a	+	+	+	+	56-23-5	CARBON TETRACHLORIDE
2.3 ^{af}	NT	+	+	NT	NT	60391-92-6	CARBOXYMETHYLNITROSOUREA
1490 ^a	NT	+	B+	NT	NT	---	CARRAGEENAN, ACID-DEGRADED
-	5230	-	-	A	+	133-90-4	CHLORAMBEN
1.41 ^d	0.097 ^{ad}	+	NT	+	+	305-03-3	CHLORAMBUCIL
-	2.15 ^a	-	-	+	+	57-74-9	CHLORDANE
110 ^a	86.8 ^a	+	+	+	+	63449-39-8	CHLORINATED PARAFFINS (C12, 60% CHLORINE)
-	6540	-	E	+	E	63449-39-8	CHLORINATED PARAFFINS (C23, 43% CHLORINE)
37.6	346	+	NT	-	+	101-79-1	4-CHLORO-4'-AMINODIPHENYLETHYR
4.85	NT	+	NT	NT	NT	24358-29-0	2-CHLORO-5-(3,5-DIMETHYLPYPERIDINOSULPHONYL) BENZOIC ACID
-	108 ^a	-	NT	+	+	88-73-3	1-CHLORO-2-NITROBENZENE
-	430 ^a	-	NT	+	+	100-00-5	1-CHLORO-4-NITROBENZENE
315	1230	+	-	-	+	5131-60-2	4-CHLORO-m-PHENYLENEDIAMINE
197 ^a	957 ^a	+	+	+	+	95-83-0	4-CHLORO-o-PHENYLENEDIAMINE
-	134 ^a	-	-	+	+	95-79-4	5-CHLORO-o-TOLUIDINE
-	15.4 ^{af}	-	-	+	+	3165-93-3	4-CHLORO-o-TOLUIDINE.HCl
7.47 ^{ac}	10.8 ^c	+	NT	+	NT	50892-23-4	[4-CHLORO-6-(2,3-XYLIDINO)-2-PYRIMIDINYLTHTIO] ACETIC ACID
6.49	44.6	+	NT	NT	+	---	4-CHLORO-6-(2,3-XYLIDINO)-2-PYRIMIDINYLTHTIO(N-beta-HYDROXYETHYL)ACETAMIDE
-	43.8 ^{af}	-	-	+	+	510-15-6	CHLOROBENZILATE
119	48 ^a	+	-	+	+	67-66-3	CHLOROFORM
5.5	NT	+	NT	NT	NT	107-30-2	CHLOROMETHYL METHYL ETHER
433	161 ^a	+	-	+	+	6959-48-4	3-(CHLOROMETHYL)PYRIDINE.HCl
8.78	NT	+	NT	NT	NT	10473-70-8	1-(4-CHLOROPHENYL)-1-PHENYL-2-PROPYNYL CARBAMATE
NT	12.9	NT	NT	-	+	683-50-1	2-CHLOROPROPANAL
NT	5.05	NT	NT	-	+	590-21-6	1-CHLOROPROPENE
2080 ^a	-	+	+	-	-	1897-45-6	CHLOROTHALONIL
0.0241 ^{ad}	NT	+	+	NT	NT	54749-90-5	CHLOROZOTOCIN
7000	2470 ^a	+	-	+	+	87-29-6	CINNAMYL ANTHRANILATE
1.09 ^c	NT	+	NT	NT	NT	52214-84-3	CIPROFIBRATE

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Table 1. (Continued)

Rat	Mouse	MR	FR	MM	FM	CAS	Name
5.28 ^{ac}	NT	+	NT	NT	NT	518-75-2	CITRININ
0.5	NT	B+	B+	NT	NT	33979-15-6	CLIVORINE
169	NT	+	NT	NT	NT	637-07-0	CLOFIBRATE
157 ^b	NT	+	NT	NT	NT	55600-34-5	CLOPHEN A 30
470 ^a	—	+	+	I	—	102-50-1	m-CRESIDINE
76.3 ^a	44.7 ^a	+	+	+	+	120-71-8	p-CRESIDINE
5.33 ^a	253 ^a	+	+	+	+	135-20-6	CUPFERRON
—	587 ^a	B—	B—	+	+	139-05-9	CYCLAMATE, SODIUM
NT	23.6	NT	NT	+	NT	12663-46-6	CYCLOCHLOROTINE
1.26 ^{aef}	5.78 ^{ad}	+	+	+	+	50-18-0	CYCLOPHOSPHAMIDE
1.05 ^a	—	+	+	—	—	16170-75-5	CYTEMBENA
0.71	0.595 ^{ad}	NT	+	+	+	4342-03-4	DACARBAZINE
1840 ^b	880 ^a	—	+	+	+	1596-84-5	DAMINOZIDE
22.4	—	+	—	—	—	80-08-0	DAPSONE
—	24.9 ^a	A	—	+	+	72-54-8	p,p'-DDD
—	9.45 ^a	—	—	+	+	72-55-9	p,p'-DDE
57.2 ^a	4.55 ^{af}	+	+	+	+	50-29-3	DDT
182 ^a	NT	+	+	NT	NT	9011-18-1	DEXTRAN SULFATE SODIUM (DS-M-1)
19	NT	NT	+	NT	NT	---	N-1-DIACETAMIDOFLUORENE
NT	19.4 ^a	NT	NT	+	—	2303-16-4	DIALATE
NT	25.7 ^a	NT	NT	+	+	5164-11-4	1,1-DIALLYLHYDRAZINE
NT	33.8 ^a	NT	NT	+	+	---	1,2-DIALLYLHYDRAZINE.2HCl
1.71	NT	NT	+	NT	NT	720-69-4	4,6-DIAMINO-2-(5-NITRO-2-FURYL)-s-TRIAZINE
72.6 ^a	791 ^a	+	+	+	+	39156-41-7	2,4-DIAMINOANISOLE SULFATE
1.43 ^a	26.7	+	+	—	+	95-80-7	2,4-DIAMINOTOLUENE
4.42	201 ^a	+	NT	+	+	636-23-7	2,4-DIAMINOTOLUENE.2HCl
NT	5.88	NT	NT	+	NT	53-70-3	DIBENZ(a,h)ANTHRACENE
2.48	NT	+	NT	NT	NT	4106-66-5	3-DIBENZOFURANAMINE
0.106 ^a	1.28 ^a	+	+	+	+	96-12-8	1,2-DIBROMO-3-CHLOROPROPANE
8.37 ^d	9.23 ^{ad}	+	NT	+	+	10318-26-0	DIBROMODULCITOL
1.1 ^a	2.34 ^a	+	+	+	+	106-93-4	1,2-DIBROMOETHANE
24.9 ^{ad}	11.4 ^{ad}	+	+	+	+	488-41-5	DIBROMOMANNITOL
4.28	NT	NT	+	NT	NT	56654-52-5	1,3-DIBUTYL-1-NITROSOUREA
NT	119	NT	NT	+	NT	23950-58-5	3,5-DICHLORO(N-1,1-DIMETHYL-2-PROPYNYL)BENZAMIDE
—	737 ^a	—	—	+	+	609-20-1	2,6-DICHLORO-p-PHENYLENEDIAMINE
3.34 ^a	0.466 ^a	+	+	+	+	7572-29-4	DICHLOROACETYLENE
18.3 ^a	NT	+	+	NT	NT	91-94-1	3,3'-DICHLOROBENZIDINE
NT	1.52 ^d	NT	NT	NT	+	110-57-6	trans-1,4-DICHLOROBUTENE-2
5.49 ^a	61.2 ^a	+	+	+	+	107-06-2	1,2-DICHLOROETHANE
—	32.9	—	—	+	—	115-32-2	DICOFOL
—	0.469 ^{ac}	—	—	+	+	60-57-1	DIELDRIN
1.63 ^c	NT	+	NT	NT	NT	7347-49-1	N,N-DIETHYL-4-(4'-PYRIDYL-1'-OXIDE)AZOANILINE
8.85 ^b	NT	+	NT	NT	NT	685-91-6	DIETHYLACETAMIDE
1660	NT	+	NT	NT	NT	111-46-6	DIETHYLENE GLYCOL
0.114	0.026 ^a	+	—	+	+	56-53-1	DIETHYLSTILBESTROL
23.8 ^a	—	+	+	—	—	105-55-5	N,N'-DIETHYLTHIOUREA
NT	571 ^a	NT	NT	+	+	628-36-4	1,2-DIFORMYLHYDRAZINE
NT	852 ^a	NT	NT	+	+	21626-89-1	DIFTALONE
1.53	NT	NT	+	NT	NT	33389-33-2	1,2-DIHYDRO-2-(5-NITRO-2-THIENYL)QUINAZOLIN-4(3H)-ONE
90.6	NT	B+	B+	NT	NT	3276-41-3	3,6-DIHYDRO-2-NITROSO-2H-1,2-OXAZINE
143	90 ^a	B+	B+	+	+	94-58-6	DIHYDROSAFROLE
716	NT	+	NT	NT	NT	828-00-2	DIMETHOXANE
0.721	95.9	+	NT	+	—	5803-51-0	2,5-DIMETHOXY-4'-AMINOSTILBENE
742 ^a	—	+	+	—	—	91-93-0	3,3'-DIMETHOXYBENZIDINE-4,4'-DIISOCYANATE
3.31	NT	NT	+	NT	NT	60-11-7	N,N-DIMETHYL-4-AMINOAZOBENZENE
105	—	+	E	—	—	868-85-9	DIMETHYL HYDROGEN PHOSPHITE
1.39 ^c	NT	NT	+	NT	NT	59-35-8	4,6-DIMETHYL-2-(5-NITRO-2-FURYL)PYRIMIDINE
17	NT	NT	+	NT	NT	551-92-8	1,2-DIMETHYL-5-NITROIMIDAZOLE
22.4	NT	NT	+	NT	NT	55738-54-0	trans-2-[(DIMETHYLAMINO)METHYLIMINO]-5-[2-(5-NITRO-2-FURYL)VINYL]-1,3,4-OXADIAZOLE
NT	0.084	NT	NT	NT	+	57-97-6	7,12-DIMETHYLBENZ(a)ANTHRACENE
NT	5.37 ^d	NT	NT	NT	+	79-44-7	DIMETHYLCARBAMYL CHLORIDE
NT	2.09 ^a	NT	NT	+	+	57-14-7	1,1-DIMETHYLHYDRAZINE
NT	0.102 ^a	NT	NT	+	+	306-37-6	1,2-DIMETHYLHYDRAZINE.2HCl

(Continued on next page)

Table 1. (Continued)

Rat	Mouse	MR	FR	MM	FM	CAS	Name
0.41 ^c	NT	NT	+	NT	NT	26049-69-4	2-(2,2-DIMETHYLHYDRAZINO)-4-(5-NITRO-2-FURYL)THIAZOLE
0.256 ^a	NT	+	+	NT	NT	4164-28-7	DIMETHYLNITRAMINE
0.0297 ^a	NT	NT	+	NT	NT	55557-00-1	DINITROSOHOMOPIPERAZINE
NT	2.01 ^a	NT	NT	+	+	140-79-4	DINITROSOPIPERAZINE
126 ^{af}	594 ^a	+	+	+	+	123-91-1	1,4-DIOXANE
NT	547 ^a	NT	NT	+	+	68-89-3	DIPYRONE
NT	0.151 ^{af}	NT	NT	-	+	8015-30-3	ENOVID
NT	0.282 ^b	NT	NT	NT	+	50-28-2	ESTRADIOL
-	0.682 ^a	-	-	+	+	22966-79-6	ESTRADIOL MUSTARD
NT	51.8	NT	NT	NT	+	140-67-0	ESTRAGOLE
-	69.3	-	-	-	+	536-33-4	ETHIONAMIDE
4.97 ^c	NT	+	NT	NT	NT	13073-35-3	ETHIONINE
5.24 ^a	NT	+	NT	NT	NT	67-21-0	DL-ETHIONINE
9110	-	+	-	NT	-	64-17-5	ETHYL ALCOHOL
NT	2.49 ^a	NT	NT	+	+	74920-78-8	N-ETHYL-N-FORMYLHYDRAZINE
NT	2.84	NT	NT	B+	B+	63885-23-4	N-ETHYL-N'-NITRO-N-NITROSOGUANIDINE
0.904 ^a	NT	+	+	NT	NT	759-73-9	1-ETHYL-1-NITROSOUREA
NT	0.283 ^a	NT	NT	+	+	151-56-4	ETHYLENE IMINE
7.43 ^{af}	NT	+	+	NT	NT	75-21-8	ETHYLENE OXIDE
10.8 ^a	16.9	+	+	+	-	96-45-7	ETHYLENE THIOUREA
-	3050 ^a	-	-	+	+	103-23-1	DI(2-ETHYLHEXYL)ADIPATE
2280 ^a	3400 ^a	+	+	+	+	117-81-7	DI(2-ETHYLHEXYL)PHTHALATE
NT	5.22 ^a	NT	NT	+	+	18413-14-4	ETHYLHYDRAZINE.HCl
2.91 ^a	NT	+	+	NT	NT	38434-77-4	ETHYLNITROSOCYANAMIDE
NT	15.3 ^a	NT	NT	NT	+	842-00-2	4-ETHYLSULPHONYLNAPHTHALENE-1-SULFONAMIDE
1.62	NT	NT	+	NT	NT	363-17-7	N-(2-FLUORENYL)-2,2,2-TRIFLUOROACETAMIDE
NT	1.09 ^a	NT	NT	+	+	324-93-6	4'-FLUORO-4-AMINODIPHENYL
1.01	NT	+	NT	NT	NT	398-32-3	N-4-(4'-FLUOROBIPHENYL)ACETAMIDE
26.5 ^a	NT	+	+	NT	NT	593-70-4	FLUOROCARBON 31
60 ^a	NT	+	+	NT	NT	75-88-7	FLUOROCARBON 133a
0.798 ^a	43.9	+	+	+	-	50-00-0	FORMALDEHYDE
14.4	NT	NT	+	NT	NT	32852-21-4	FORMIC ACID 2-(4-METHYL-2-THIAZOLYL)HYDRAZIDE
3.54 ^a	8.85 ^a	+	+	NT	+	3570-75-0	FORMIC ACID 2-[4-(5-NITRO-2-FURYL)-2-THIAZOLYL]HYDRAZIDE
NT	36 ^a	NT	NT	+	+	624-84-0	FORMYLHYDRAZINE
3920 ^a	-	+	+	-	-	4680-78-8	FD & C GREEN NO. 1
5640	-	B+	B+	-	-	5141-20-8	FD & C GREEN NO. 2
NT	1660 ^b	NT	NT	+	-	126-07-8	GRISEOFULVIN
5.96E-4	8.76E-4 ^a	-	+	+	+	mixture	HCDD MIXTURE
1000	NT	B+	B+	NT	NT	517-28-2	HEMATOXYLIN
-	1.09 ^a	-	-	+	+	76-44-8	HEPTACHLOR
1.65 ^c	46.4 ^a	NT	+	+	+	118-74-1	HEXACHLOROBENZENE
50.5 ^a	NT	+	+	NT	NT	87-68-3	HEXACHLOROBUTADIENE
NT	25.3	NT	NT	+	NT	608-73-1	HEXACHLOROCYCLOHEXANE
11.2	6.62 ^c	+	NT	+	NT	319-84-6	alpha-1,2,3,4,5,6-HEXACHLOROCYCLOHEXANE
NT	17.7 ^a	NT	NT	+	+	319-85-7	beta-1,2,3,4,5,6-HEXACHLOROCYCLOHEXANE
-	15.4 ^a	-	-	+	+	58-89-9	gamma-1,2,3,4,5,6-HEXACHLOROCYCLOHEXANE
-	319 ^a	-	-	+	+	67-72-1	HEXACHLOROETHANE
10.2	NT	NT	+	NT	NT	531-18-0	HEXAMETHYLMELAMINE
-	1950	-	-	+	-	628-02-4	HEXANAMIDE
NT	2.2 ^a	NT	NT	+	+	302-01-2	HYDRAZINE
39.4 ^a	3.35 ^{af}	+	+	+	+	10034-93-2	HYDRAZINE SULFATE
1.03	11.3	NT	+	NT	+	26049-71-8	2-HYDRAZINO-4-(p-AMINOPHENYL)THIAZOLE
2.83 ^a	16.4	NT	+	NT	+	26049-68-3	2-HYDRAZINO-4-(5-NITRO-2-FURYL)THIAZOLE
1.97 ^a	10.6	NT	+	NT	+	26049-70-7	2-HYDRAZINO-4-(p-NITROPHENYL)THIAZOLE
3.55 ^a	26	+	+	-	+	122-66-7	HYDRAZOBENZENE
NT	9010	NT	NT	B+	B+	7722-84-1	HYDROGEN PEROXIDE
6.9E-4 ^a	6.23	+	+	NT	+	53-95-2	N-HYDROXY-2-ACETYLAMINOFLUORENE
NT	57.8	NT	NT	NT	+	51410-44-7	1'-HYDROXYESTRAGOLE
16.7	NT	NT	+	NT	NT	5036-03-3	1-(2-HYDROXYETHYL)-3-[(5-NITROFURFURYLIDENE)AMINO]-2-IMIDAZOLIDINONE
1.52	NT	+	NT	NT	NT	13743-07-2	1-(2-HYDROXYETHYL)-1-NITROSOUREA
1.87	NT	NT	+	NT	NT	33389-36-5	4-(2-HYDROXYETHYLAMINO)-2-(5-NITRO-2-THIENYL)QUINAZOLINE

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Table 1. (Continued)

Rat	Mouse	MR	FR	MM	FM	CAS	Name
NT	0.314 ^a	NT	NT	+	-	109-84-2	2-HYDROXYETHYLHYDRAZINE
12.1 ^a	49.1 ^a	+	NT	+	+	5208-87-7	1'-HYDROXYSAFROLE
10.7 ^d	23.7 ^d	-	+	-	+	21416-87-5	ICRF-159
120 ^a	11.2 ^{af}	+	+	+	+	54-85-3	ISONIAZID
NT	27.4	NT	NT	B+	B+	149-17-7	ISONICOTINIC ACID VANILLYLIDENEHYDRAZIDE
0.739 ^d	5.06 ^d	-	+	-	+	3778-73-2	ISOPHOSPHAMIDE
2.96	0.705 ^a	-	+	+	+	143-50-0	KEPONE
0.141 ^a	NT	+	+	NT	NT	303-34-4	LASIOCARPINE
107 ^a	472 ^a	+	+	+	+	1335-32-6	LEAD ACETATE, BASIC
NT	55.8	NT	NT	+	-	24365-47-7	LEUPEPTIN
NT	14.8 ^a	NT	NT	+	+	21884-44-6	LUTEOSKYRIN
NT	14.1	NT	NT	NT	+	24382-04-5	MALONALDEHYDE, SODIUM
157	-	B+	B+	-	-	12427-38-2	MANGANESE ETHYLENEBISTHIOCARBAMATE
735	-	+	-	-	-	108-78-1	MELAMINE
0.0719 ^{ad}	0.137 ^{ad}	+	+	+	+	148-82-3	MELPHALAN
4.46	NT	+	NT	NT	NT	57-39-6	METAPA
7.65 ^a	NT	+	+	NT	NT	135-23-9	METHAPYRILENE.HCl
0.9 ^a	NT	+	+	NT	NT	60-56-0	METHIMAZOLE
NT	60.2	NT	NT	-	+	3544-23-8	3-METHOXY-4-AMINOAZOBENZENE
25.7 ^a	NT	+	+	NT	NT	5834-17-3	2-METHOXY-3-AMINODIBENZOFURAN
9.17 ^c	NT	+	NT	NT	NT	21340-68-1	METHYL CLOFENAPATE
NT	8.03	NT	NT	B+	B+	---	1-METHYL-1,4-DIHYDRO-7-[2-(5-NITROFURYL)VINYL]-4-OXO-1,8-NAPHTHYRIDINE-3-CARBOXYLATE, POTASSIUM
1.3 ^{bd}	NT	+	NT	NT	NT	99-80-9	N-METHYL-N,4-DINITROSOANILINE
NT	0.745 ^{af}	NT	NT	+	+	758-17-8	N-METHYL-N-FORMYLHYDRAZINE
NT	31.8	NT	NT	+	NT	66-27-3	METHYL METHANESULFONATE
0.523 ^a	NT	+	+	NT	NT	70-25-7	N-METHYL-N'-NITRO-N-NITROSOGUANIDINE
48.8 ^a	1.34 ^a	+	+	+	+	129-15-7	2-METHYL-1-NITROANTHRAQUINONE
5.34	NT	NT	+	NT	NT	21638-36-8	4-METHYL-1-[(5-NITROFURFURYLIDENE)AMINO]-2-IMIDAZOLIDINONE
0.468 ^a	NT	+	+	NT	NT	16699-10-8	4-(4-N-METHYL-N-NITROSAMINOSTYRYL)QUINOLINE
3.23 ^a	NT	+	+	NT	NT	63412-06-6	N-METHYL-N-NITROSOBENZAMIDE
0.633 ^{ad}	NT	+	+	NT	NT	---	N-(N-METHYL-N-NITROSOCARBAMOYL)-L-ORNITHINE
20.4	NT	B+	B+	NT	NT	14026-03-0	R(-)-2-METHYL-N-NITROSOPIPERIDINE
13.2	NT	B+	B+	NT	NT	36702-44-0	S(+)-2-METHYL-N-NITROSOPIPERIDINE
0.202 ^a	NT	-	+	NT	NT	56-49-5	3-METHYLCHOLANTHRENE
9.09 ^a	NT	+	+	NT	NT	101-14-4	4,4'-METHYLENE-BIS(2-CHLOROANILINE)
-	66.6	-	NT	-	+	64049-29-2	4,4'-METHYLENE-BIS(2-CHLOROANILINE).2HCl
6.91 ^a	NT	+	+	NT	NT	838-88-0	4,4'-METHYLENE-BIS(2-METHYLANILINE)
598	817 ^a	A	+	+	+	75-09-2	METHYLENE CHLORIDE
16.4 ^a	207	+	+	-	+	101-61-1	4,4'-METHYLENEBIS(N,N-DIMETHYL)BENZENAMINE
12.5 ^a	22.3 ^a	+	+	+	+	13552-44-8	4,4'-METHYLENEDIANILINE.2HCl
NT	4.58 ^a	NT	NT	+	+	60-34-4	METHYLHYDRAZINE
NT	2.51 ^a	NT	NT	+	+	302-15-8	METHYLHYDRAZINE SULFATE
NT	18	NT	NT	+	-	---	(N-6)-(METHYLNITROSO)ADENINE
NT	15.8 ^a	NT	NT	+	+	---	(N-6)-(METHYLNITROSO)ADENOSINE
0.48	NT	NT	+	NT	NT	33868-17-6	METHYLNITROSOCYANAMIDE
431 ^a	347 ^a	+	+	+	+	443-48-1	METRONIDAZOLE
4.87 ^a	53 ^a	+	+	+	+	90-94-8	MICHLER'S KETONE
-	1.1 ^a	-	NT	+	+	2385-85-5	MIREX
1.46	NT	+	NT	NT	NT	39801-14-4	MIREX, PHOTO-
9.81E-4 ^{ad}	NT	+	+	NT	NT	50-07-7	MITOMYCIN-C
NT	4.48 ^a	NT	NT	+	+	1068-57-1	MONOACETYL HYDRAZINE
0.79 ^a	NT	+	NT	NT	NT	315-22-0	MONOCROTALINE
5.03	NT	NT	+	NT	NT	58139-48-3	4-MORPHOLINO-2-(5-NITRO-2-THIENYL)QUINAZOLINE
6.33	NT	NT	+	NT	NT	3031-51-4	L-5-MORPHOLINOMETHYL-3-[(5-NITROFURFURYLIDENE)AMINO]-2-OXAZOLIDINONE.HCl
50.8	66.6 ^a	-	+	+	+	2243-62-1	1,5-NAPHTHALENEDIAMINE
61.6	20.5 ^a	B-	+	B+	+	91-59-8	2-NAPHTHYLAMINE
NT	145 ^a	NT	NT	+	+	553-53-7	NICOTINIC ACID HYDRAZIDE
131	758	-	+	+	-	139-94-6	NITHIAZIDE
1450 ^a	1470 ^a	+	+	+	+	139-13-9	NITRILOTRIACETIC ACID
224 ^a	-	+	+	-	-	18662-53-8	NITRILOTRIACETIC ACID, TRISODIUM SALT, MONOHYDRATE

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Table 1. (Continued)

Rat	Mouse	MR	FR	MM	FM	CAS	Name
124 ^a	—	+	+	—	—	7632-00-0	NITRITE, SODIUM
—	2270	—	—	+	—	1777-84-0	3-NITRO-p-ACETOPHENETIDE
28.1 ^a	3720	+	+	—	+	99-59-2	5-NITRO-o-ANISIDINE
4.64 ^{ac}	NT	NT	+	NT	NT	59-87-0	5-NITRO-2-FURALDEHYDE SEMICARBAZONE
11.9 ^a	20.3 ^{ac}	+	+	+	+	75198-31-1	3-(5-NITRO-2-FURYL)-IMIDAZO(1,2- α)PYRIDINE
8.61	NT	NT	+	NT	NT	2122-86-3	5-(5-NITRO-2-FURYL)-1,3,4-OXADIAZOLE-2-OL
59.6 ^b	NT	NT	+	NT	NT	36133-88-7	N-[3-(5-NITRO-2-FURYL)-1,2,4-OXADIAZOLE-5-YL]-METHYLACETAMIDE
8.84	6.74	NT	+	NT	+	2578-75-8	N-[5-(5-NITRO-2-FURYL)-1,3,4-THIADIAZOL-2-YL]ACETAMIDE
7.68	NT	NT	+	NT	NT	53757-28-1	4-(5-NITRO-2-FURYL)THIAZOLE
10.5 ^a	NT	NT	+	NT	NT	531-82-8	N-[4-(5-NITRO-2-FURYL)-2-THIAZOLYL]ACETAMIDE
1.31 ^{af}	7.72 ^a	+	+	+	+	24554-26-5	N-[4-(5-NITRO-2-FURYL)-2-THIAZOLYL]FORMAMIDE
14.1	NT	NT	+	NT	NT	51325-35-0	N,N'-[6-(5-NITRO-2-FURYL)-s-TRIAZINE-2,4-DIYL]BISACETAMIDE
8.66	0.346	B+	B+	B+	B+	4812-22-0	3-NITRO-3-HEXENE
—	614	—	—	—	+	5307-14-2	2-NITRO-p-PHENYLENEDIAMINE
—	242 ^a	—	—	+	+	99-55-8	5-NITRO-o-TOLUIDINE
5.98 ^a	45.3	+	+	—	+	602-87-9	5-NITROACENAPHTHENE
—	354 ^a	—	—	+	+	94-52-0	6-NITROBENZIMIDAZOLE
420	64.2 ^a	I	+	+	+	1836-75-5	NITROFEN
5.26	NT	NT	+	NT	NT	555-84-0	1-[5-NITROFURFURYLIDENE)AMINO]-2-IMIDAZOLIDINONE
0.0114 ^d	NT	+	NT	NT	NT	51-75-2	NITROGEN MUSTARD
0.764 ^d	NT	+	NT	NT	NT	126-85-2	NITROGEN MUSTARD N-OXIDE
9.55 ^a	NT	+	+	NT	NT	607-35-2	8-NITROQUINOLINE
0.364	NT	+	NT	NT	NT	38777-13-8	NITROSO-BAYGON
0.707 ^a	NT	+	+	NT	NT	---	N-NITROSO-BIS-(4,4,4-TRIFLUORO-N-BUTYL)AMINE
0.0932 ^a	NT	+	+	NT	NT	16813-36-8	1-NITROSO-5,6-DIHYDROURACIL
0.0535	NT	NT	+	NT	NT	89911-79-5	N-NITROSO-2,3-DIHYDROXYPROPYL-2-HYDROXYPROPYLAMINE
0.0352	NT	NT	+	NT	NT	92177-50-9	NITROSO-2,3-DIHYDROXYPROPYL-2-OXOPROPYLAMINE
5.98	NT	NT	+	NT	NT	89911-78-4	N-NITROSO-2,3-DIHYDROXYPROPYLETHANOLAMINE
9.66	NT	NT	+	NT	NT	61034-40-0	1-NITROSO-3,5-DIMETHYL-4-BENZOYLPIPERAZINE
1.02	NT	NT	+	NT	NT	75896-33-2	N-NITROSO-(2-HYDROXYPROPYL)-(2-HYDROXYETHYL)AMINE
7.65	NT	B+	B+	NT	NT	56222-35-6	N-NITROSO-3-HYDROXYPYRROLIDINE
4.73	NT	NT	+	NT	NT	760-60-1	N-NITROSO-N-ISOBUTYLUREA
0.487 ^a	NT	+	+	NT	NT	55090-44-3	N-NITROSO-N-METHYL-N-DODECYLAMINE
0.255	NT	+	NT	NT	NT	937-25-7	N-NITROSO-N-METHYL-4-FLUOROANILINE
0.00788 ^a	NT	+	NT	NT	NT	13256-11-6	NITROSO-N-METHYL-N-(2-PHENYL)ETHYLAMINE
29.4 ^c	NT	+	NT	NT	NT	75881-20-8	N-NITROSO-N-METHYL-N-TETRADECYLAMINE
1.26	NT	+	NT	NT	NT	75881-22-0	N-NITROSO-N-METHYLDECYLAMINE
1.8	NT	NT	+	NT	NT	92177-49-6	NITROSO-2-OXOPROPYLETHANOLAMINE
0.166 ^d	NT	+	NT	NT	NT	15973-99-6	DI(N-NITROSO)-PERHYDROPYRIMIDINE
0.0374 ^a	NT	NT	+	NT	NT	55556-92-8	NITROSO-1,2,3,6-TETRAHYDROPYRIDINE
2.52	NT	+	NT	NT	NT	82018-90-4	N-NITROSO(2,2,2-TRIFLUOROETHYL)ETHYLAMINE
3.31 ^d	NT	+	NT	NT	NT	29929-77-9	N-NITROSO-2,2,4-TRIMETHYL-1,2-DIHYDROQUINOLINE POLYMER
0.151	NT	NT	+	NT	NT	75881-18-4	1-NITROSO-3,4,5-TRIMETHYLPIPERAZINE
0.825	NT	NT	+	NT	NT	88208-16-6	N-NITROSOALLYL-2,3-DIHYDROXYPROPYLAMINE
0.877	NT	NT	+	NT	NT	91308-70-2	N-NITROSOALLYL-2-HYDROXYPROPYLAMINE
0.335	NT	NT	+	NT	NT	91308-71-3	N-NITROSOALLYL-2-OXOPROPYLAMINE
0.491	NT	NT	+	NT	NT	91308-69-9	N-NITROSOALLYLETHANOLAMINE
1.01	NT	NT	+	NT	NT	---	NITROSOAMYLURETHAN
11 ^a	NT	+	+	NT	NT	1133-64-8	NITROSOANABASINE
1.13	NT	B+	B+	NT	NT	51542-33-7	N-NITROSOBENZTHIAZURON
0.813 ^a	NT	+	+	NT	NT	53609-64-6	N-NITROSOBIS(2-HYDROXYPROPYL)AMINE
0.232 ^a	NT	+	+	NT	NT	60599-38-4	N-NITROSOBIS(2-OXOPROPYL)AMINE
0.691	1.09	+	NT	+	NT	924-16-3	NITROSODIBUTYLAMINE
1.9 ^a	NT	+	+	NT	NT	1116-54-7	N-NITROSODIETHANOLAMINE
0.00787 ^{af}	NT	+	+	NT	NT	55-18-5	N-NITROSODIETHYLAMINE
0.0587 ^{af}	0.153 ^a	+	+	+	+	62-75-9	N-NITROSODIMETHYLAMINE
116 ^a	—	+	+	—	—	86-30-6	N-NITROSODIPHENYLAMINE
201	340	+	—	+	—	156-10-5	p-NITROSODIPHENYLAMINE
0.186	NT	NT	+	NT	NT	621-64-7	N-NITROSODIPROPYLAMINE
10.9 ^a	NT	+	+	NT	NT	40580-89-0	NITROSODECAMETHYLENEIMINE

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Table 1. (Continued)

Rat	Mouse	MR	FR	MM	FM	CAS	Name
95.2	NT	+	NT	NT	NT	17608-59-2	N-NITROSOEPHEDRINE
0.248	NT	NT	+	NT	NT	614-95-9	NITROSOETHYLURETHAN
0.0292 ^a	NT	+	NT	NT	NT	20917-49-1	NITROSOHEPTAMETHYLENEIMINE
NT	0.313 ^a	NT	NT	+	+	932-83-2	N-NITROSOHEXAMETHYLENEIMINE
43.8 ^a	NT	+	+	NT	NT	42579-28-2	1-NITROSOHYDANTOIN
0.646	NT	NT	+	NT	NT	86451-37-8	N-NITROSOMETHYL-2,3-DIHYDROXYPROPYLAMINE
0.0442 ^a	NT	+	+	NT	NT	75411-83-5	N-NITROSOMETHYL-2-HYDROXYPROPYLAMINE
0.214	NT	NT	+	NT	NT	16219-98-0	2-NITROSOMETHYLAMINOPYRIDINE
0.0343 ^{af}	NT	+	+	NT	NT	614-00-6	NITROSOMETHYLANILINE
2.37	NT	+	NT	NT	NT	68107-26-6	NITROSOMETHYLUDECYLAMINE
0.573 ^a	NT	+	+	NT	NT	78246-24-9	N'-NITROSONORNICOTINE-1-N-OXIDE
5.51 ^{ab}	NT	+	+	NT	NT	5632-47-3	N-NITROSOPIPERAZINE
1.57	1.3	B+	B+	+	NT	100-75-4	N-NITROSOPIPERIDINE
1.54 ^{ac}	NT	+	+	NT	NT	930-55-2	N-NITROSOPYRROLIDINE
4.15 ^a	NT	+	+	NT	NT	26541-51-5	N-NITROSOTHIOMORPHOLINE
50.7	NT	+	NT	NT	NT	611-23-4	o-NITROSOTOLUENE
1.94	1.34 ^b	B+	B+	NT	+	8015-12-1	NORLESTRIN
6.17	NT	NT	+	NT	NT	3096-50-2	N-(9-OXO-2-FLUORENYL)ACETAMIDE
6.65 ^a	19.7 ^a	+	+	+	+	101-80-4	4,4'-OXYDIANILINE
-	39.8 ^a	A	-	+	+	76-01-7	PENTACHLOROETHANE
-	71.1	-	-	+	-	82-68-8	PENTACHLORONITROBENZENE
NT	5.87	NT	NT	-	+	1119-68-2	n-PENTYLHYDRAZINE.HCl
0.662 ^a	NT	+	+	NT	NT	60102-37-6	PETASITENINE
741 ^a	1100 ^{af}	+	+	+	+	62-44-2	PHENACETIN
1230	NT	+	NT	NT	NT	60-80-0	PHENAZONE
303 ^a	71.1	+	+	-	+	136-40-3	PHENAZOPYRIDINE.HCl
0.523	0.211 ^a	-	+	+	+	3546-10-9	PHENESTERIN
-	4.18 ^a	-	-	+	+	50-06-6	PHENOBARBITAL
74.3 ^a	34.6 ^a	+	+	+	+	57-30-7	PHENOBARBITAL, SODIUM
0.71 ^{ad}	4.95 ^{ad}	+	+	+	+	63-92-3	PHENOXYBENZAMINE.HCl
2.31	NT	B+	B+	NT	NT	7227-91-0	1-PHENYL-3,3-DIMETHYLTRIAZENE
17.7 ^a	-	+	+	-	-	842-07-9	1-PHENYLazo-2-NAPHTHOL
248	611 ^a	+	NT	+	+	615-28-1	o-PHENYLENEDIAMINE.2HCl
NT	14.6	NT	NT	-	+	156-51-4	PHENYLETHYLHYDRAZINE SULFATE
29.1 ^a	NT	+	+	NT	NT	122-60-1	PHENYLGLYCIDYL ETHER
NT	70.6 ^a	NT	NT	+	+	59-88-1	PHENYLHYDRAZINE.HCl
414	-	+	NT	-	-	132-27-4	o-PHENYLPHENATE, SODIUM
232	-	+	NT	-	-	90-43-7	o-PHENYLPHENOL
NT	2.21 ^d	NT	NT	-	+	17673-25-5	PHORBOL
-	62.2	-	-	+	-	120-62-7	PIPERONYL SULFOXIDE
154 ^a	-	+	+	-	-	1955-45-9	PIVALOLACTONE
0.148 ^a	0.381 ^a	+	+	+	+	67774-32-7	POLYBROMINATED BIPHENYL MIXTURE
4.01 ^d	NT	+	NT	NT	NT	671-16-9	PROCARBAZINE
0.284 ^{ad}	0.194 ^{ad}	+	+	+	+	366-70-1	PROCARBAZINE.HCl
3.64 ^a	NT	+	+	NT	NT	1120-71-4	PROPANE SULTONE
1.34 ^a	1.16 ^a	NT	+	+	+	57-57-8	beta-PROPIOLACTONE
NT	8.74 ^a	NT	NT	+	+	77337-54-3	N-N'-PROPYL-N-FORMYLHYDRAZINE
0.919 ^a	NT	+	NT	NT	NT	13010-07-6	N-PROPYL-N'-NITRO-N-NITROGUANIDINE
35.1 ^a	732 ^a	+	+	+	+	75-56-9	1,2-PROPYLENE OXIDE
NT	41.4 ^a	NT	NT	+	+	56795-66-5	PROPYLHYDRAZINE.HCl
10.3 ^a	409	+	+	B+	B+	51-52-5	PROPYLTHIOURACIL
24500	NT	B+	B+	NT	NT	2611-82-7	SX PURPLE
175 ^a	NT	+	+	NT	NT	59-33-6	PYRILAMINE MALEATE
5.12 ^a	-	+	+	-	-	117-39-5	QUERCETIN
106	-	-	+	-	-	105-11-3	p-QUINONE DIOXIME
233 ^a	659 ^a	+	+	+	+	3761-53-3	D & C RED NO. 5
104	-	+	A	-	-	5160-02-1	D & C RED NO. 9
225 ^{af}	NT	+	+	NT	NT	3564-09-8	FD & C RED NO. 1
632 ^a	NT	B+	B+	NT	NT	915-67-3	FD & C RED NO. 2
6130 ^a	-	B+	B+	B-	B-	4548-53-2	FD & C RED NO. 4
0.306	3.58 ^a	+	-	+	+	50-55-5	RESERPINE
-	33.6	-	-	-	+	13292-46-1	RIFAMPICIN
-	67.8 ^a	-	-	+	+	26308-28-1	RIPAZEPAM
21.2 ^a	28.8 ^a	+	+	+	+	569-61-9	p-ROSANILINE.HCl
1110 ^{af}	-	+	-	-	-	128-44-9	SACCHARIN, SODIUM

(Continued on next page)

Table 1. (Continued)

Rat	Mouse	MR	FR	MM	FM	CAS	Name
340 ^a	27 ^a	+	B+	+	+	94-59-7	SAFROLE
44.6	NT	NT	+	NT	NT	18559-94-9	SALBUTAMOL
NT	1.49	NT	NT	+	-	5456-28-0	SELENIUM DIETHYLDITHIOCARBAMATE
6.14 ^a	46.8	+	+	-	+	7446-34-6	SELENIUM SULFIDE
1.7 ^d	NT	+	NT	NT	NT	2318-18-5	SENKIRKINE
0.0825 ^{af}	0.689 ^a	+	B+	NT	+	10048-13-2	STERIGMATOCYSTIN
0.776 ^a	0.193 ^{ad}	+	+	+	+	18883-66-4	STREPTOZOTOCIN
NT	0.644 ^a	NT	NT	+	-	8001-50-1	STROBANE
63 ^a	NT	+	+	NT	NT	96-09-3	STYRENE OXIDE
17.2 ^a	27.3 ^a	+	+	+	+	95-06-7	SULFALLATE
55.6 ^b	NT	NT	+	NT	NT	77-46-3	4,4'-SULFONYLBISACETANILIDE
1.91 ^d	NT	+	NT	NT	NT	22571-95-5	SYMPHYTINE
33.2	36.3	+	A	I	+	542-75-6	TELONE II
410	NT	NT	+	NT	NT	23031-25-6	TERBUTALINE
395	288	+	NT	+	-	7411-49-6	3,3',4,4'-TETRAAMINOBIPHENYL.4HCl
6.67E-6 ^{af}	8.68E-5 ^a	+	+	+	+	1746-01-6	2,3,7,8-TETRACHLORODIBENZO-p-DIOXIN
-	175 ^a	-	-	+	+	630-20-6	1,1,1,2-TETRACHLOROETHANE
-	35.4 ^a	-	-	+	+	79-34-5	1,1,2,2-TETRACHLOROETHANE
90.8	75.6 ^a	+	A	+	+	127-18-4	TETRACHLOROETHYLENE
-	228	-	A	+	A	961-11-5	TETRACHLORVINPHOS
-	86.3	-	NT	+	-	63886-77-1	TETRAFLUORO-m-PHENYLENEDIAMINE.2HCl
24.3	NT	B+	B+	NT	NT	40548-68-3	TETRAHYDRO-2-NITROSO-2H-1,2-OXAZINE
0.122 ^{ad}	0.21 ^{ad}	+	+	+	+	52-24-4	THIO-TEPA
NT	5.36 ^a	NT	NT	+	+	62-55-5	THIOACETAMIDE
5.52 ^a	32.7 ^a	+	+	+	+	139-65-1	4,4'-THIODIANILINE
2.1 ^d	NT	A	+	I	I	64039-27-6	beta-THIOGUANINE DEOXYRIBOSIDE
NT	48.6 ^a	NT	NT	+	+	141-90-2	THIOURACIL
93.5 ^a	-	+	-	NT	-	62-56-6	THIOUREA
3960	NT	B+	B+	NT	NT	88-19-7	o-TOLUENESULFONAMIDE
-	1440 ^b	-	NT	+	-	638-03-9	m-TOLUIDINE.HCl
23.3 ^a	646 ^a	+	+	+	+	636-21-5	o-TOLUIDINE.HCl
-	49.1 ^a	-	NT	+	+	540-23-8	p-TOLUIDINE.HCl
-	206	-	-	+	-	622-51-5	p-TOLYLUREA
-	4.08 ^a	A	A	+	+	8001-35-2	TOXAPHENE
0.00504 ^d	NT	+	NT	NT	NT	68-76-8	TRENIMON
-	259	-	NT	+	-	634-93-5	2,4,6-TRICHLOROANILINE
-	47.6 ^a	-	-	+	+	79-00-5	1,1,2-TRICHLOROETHANE
-	421 ^a	-	-	+	+	79-01-6	TRICHLOROETHYLENE
405	856 ^a	+	-	+	+	88-06-2	2,4,6-TRICHLOROPHENOL
NT	100 ^a	NT	NT	+	+	102-71-6	TRIETHANOLAMINE
6.79	9.98	NT	+	NT	+	42011-48-3	2,2,2-TRIFLUORO-N-[4-(5-NITRO-2-FURYL)-2-THIAZOLYL]ACETAMIDE
-	330	-	-	-	+	1582-09-8	TRIFLURALIN
20.4 ^a	6.13	+	+	-	+	137-17-7	2,4,5-TRIMETHYLANILINE
98.5 ^b	40 ^a	+	NT	+	+	21436-97-5	2,4,5-TRIMETHYLANILINE.HCl
5.17	19.3 ^a	+	NT	+	+	6334-11-8	2,4,6-TRIMETHYLANILINE.HCl
-	335	A	-	-	+	512-56-1	TRIMETHYLPHOSPHATE
25.8	-	-	+	-	-	2489-77-2	TRIMETHYLTHIOUREA
NT	3.44 ^d	NT	NT	NT	+	38571-73-2	TRIS-1,2,3-(CHLOROMETHOXY)PROPANE
1.57 ^a	80.1 ^a	+	+	+	+	126-72-7	TRIS(2,3-DIBROMOPROPYL)PHOSPHATE
41.3	12.5 ^a	B+	B+	+	+	51-79-6	URETHANE
132 ^a	NT	+	+	NT	NT	108-05-4	VINYL ACETATE
17.9 ^a	NT	+	+	NT	NT	593-60-2	VINYL BROMIDE
3.69 ^{af}	10.6 ^a	+	+	+	+	75-01-4	VINYL CHLORIDE
-	23.6 ^a	-	-	+	+	75-35-4	VINYLDENE CHLORIDE
418 ^a	-	-	+	-	-	1694-09-3	FD & C VIOLET NO. 1
NT	39.6 ^b	NT	NT	NT	+	50-14-6	VITAMIN D2
-	12.4	-	NT	-	+	21436-96-4	2,4-XYLIDINE.HCl
152	552 ^a	+	NT	+	+	51786-53-9	2,5-XYLIDINE.HCl
380	1020	+	-	-	+	2832-40-8	C.I. DISPERSE YELLOW 3
-	10900	-	-	+	-	128-66-5	C.I. VAT YELLOW 4
-	22 ^a	-	-	+	+	17924-92-4	ZEARALENONE
25.8 ^a	-	+	B+	-	E	137-30-4	ZINC DIMETHYLDITHIOCARBAMATE
255	-	B+	B+	-	-	12122-67-7	ZINC ETHYLENEBISTHIOCARBAMATE

(Continued on next page)

Table 1. (Continued)

TD₅₀ value:

For each species, the reported TD₅₀ value is the most potent in the CPDB from among sites that a published author evaluated as positive. This TD₅₀ was selected from those with a statistically significant dose response effect (two-tailed $p < 0.1$). If no site evaluated as positive was significant, then the reported TD₅₀ was the most potent among those positive sites, and the footnote "b" indicates that $p \geq 0.1$.

Abbreviations:

- CAS = Chemical Abstracts Service registry number
- NT = No Test in the CPDB in this group
- + = The CPDB contains at least one experiment in which the compound was evaluated as a carcinogen by the published author. For NCI/NTP tests, the evaluation was "clear evidence of carcinogenicity."
- I = No tests in the CPDB in this sex-species group were evaluated as positive; however, the NCI/NTP test was evaluated as inadequate.
- A = The chemical was evaluated as a carcinogen in at least one test in the CPDB, but not in this sex-species group. However, the NCI evaluated the compound in this sex-species group as "associated with carcinogenicity" in their test, or the NTP evaluated it as having "some evidence of carcinogenicity."
- E = The chemical was evaluated as a carcinogen in at least one test in the CPDB, but not in this sex-species group. The only evidence for carcinogenicity in the CPDB for this sex-species group was an "equivocal" evaluation by the NTP.
- = The chemical was evaluated as a carcinogen in at least one test in the CPDB but all tests in this group were negative.
- B+ = In the only positive test in the sex-species, results were reported only for males and females combined.
- B- = In the only test in the sex-species, results were reported only for males and females combined, and the test was negative.

Footnotes:

- a = The CPDB contains more than one positive test in the species.
- b = The reported TD₅₀ is not statistically significant (i.e. $p \geq 0.1$), and all positively evaluated results in the species are not significant.
- c = Only an upper bound and no TD₅₀ could be estimated because all dosed animals had the tumor of interest and only summary data were available. The reported value is the 99% upper confidence limit.
- d = All positive results in the CPDB are from tests in which the compound was administered by either intraperitoneal or intravenous injection.
- e = The reported TD₅₀ is from a test in which the compound was administered by intraperitoneal or intravenous injection; however, the CPDB also contains a positive test with a less potent TD₅₀ value from a test with an oral or inhalation route.
- f = TD₅₀ values from different significant, positive experiments in this species vary by more than ten-fold from one another. The most potent TD₅₀ value is reported here.

chemicals among the 955 chemicals in the CPDB that were tested in rats or mice. The table provides information for each substance on the most potent TD_{50} value in each species, the strength of evidence for carcinogenicity in each sex-species group, and the Chemical Abstracts Service (CAS) registry number. Forty-six percent of these chemicals were tested in both rats and mice, 35% in rats only, and 19% in mice only. The positivity results for the 492 compounds can be summarized as follows: 342 are positive in rats, and 278 are positive in mice. Among the 228 carcinogens tested in both rats and mice, 100 (44%) are positive in only one species. One hundred sixty-two chemicals were tested in all four sex-species groups, and 52 (32%) of these are positive in all four. Only 133 (27%) of the carcinogens listed in Table 1 were tested in the NCI/NTP Bioassay Program. A detailed analysis of positivity and target sites in the CPDB can be found in Gold et al. (7).

The distribution of TD_{50} values in Table 1 is summarized in Figure 1. 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (86.8 ng/kg/day) and C.I. Vat Yellow 4 (10.9 g/kg/day) represent the minimum and maximum TD_{50} values for mice. 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (6.67 ng/kg/day) and SX Purple (24.5 g/kg/day) represent the minimum and maximum values for rats. Among the 128 chemicals in Table 1 that are positive in both species, the TD_{50} in rats is more potent than the value in mice for 88, and less potent for 40. Species differences in potency values (in mg/kg/day) are within a factor of 10 for 95 of the 128 compounds (74%). A similar proportion has been reported for chemicals administered in the diet, using the lowest TD_{50} per species regardless of the author's evaluation of carcinogenicity or statistical significance (12).

Discussion

Summary Measures of Carcinogenic Potency

In Table 1 we selected the TD_{50} value from one case, the most potent, to represent a chemical within a species. When more than one experiment fulfilled the selection criteria, other summary measures of TD_{50} could have been used that take into account all positive results for a compound. We evaluated three summary measures: the harmonic mean, the geometric mean, and the arithmetic mean to determine how different our results would have been had we used one of these measures. These measures differ according to the weight given outlying results. If we define, T_i , $i = 1, n$, to be the n values of TD_{50} that fulfill the selection criteria for a chemical, then the harmonic mean, T_H , is defined as

$$T_H = \frac{1}{\frac{1}{n} \sum_{i=1}^n \frac{1}{T_i}} ;$$

the geometric mean, T_G , is defined as

$$T_G = \left(\prod_{i=1}^n T_i \right)^{\frac{1}{n}} ;$$

and the arithmetic mean, T_A , is defined as

$$T_A = \frac{1}{n} \sum_{i=1}^n T_i .$$

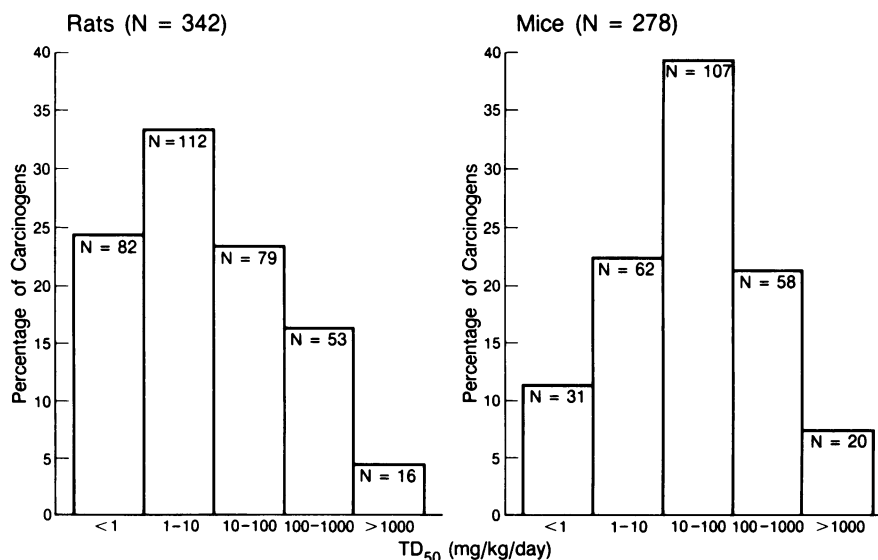


FIGURE 1. Frequency distribution of TD_{50} in the most potent site for chemicals evaluated as carcinogens in rats or mice by the author of at least one experiment.

Means based on these measures can be ordered in terms of their relationship to our most potent site, T_P :

$$T_P \leq T_H \leq T_G \leq T_A$$

Table 2 shows the distribution of values of the ratios T_H/T_P , T_G/T_P , and T_A/T_P for rats and mice for chemicals that have more than one positive test in a species; Table 2 therefore includes one-half of the rat carcinogens in Table 1 and two-thirds of those in mice. The remaining chemicals in Table 1 have only one positive test. Those compounds for which we obtained a 10-fold or greater discrepancy in these ratios are listed in the footnote to Table 2. We have selected T_P for presentation in Table 1. One could have chosen the harmonic or other forms of the mean for presentation since they take the results of all positive experiments into account. For various purposes one may wish to use different summary measures; however, as we show in Table 2, it makes little difference whether the choice is the most potent site or a mean. The TD_{50} values used to compute summary estimates can be found in Gold et al. (4-6).

Chemicals with Widely Varying TD_{50} Estimates

To further indicate particular substances for which TD_{50} values from two or more experiments differ greatly, we denote in Table 1 those chemicals for which the minimum estimate differs from the maximum estimate by more than a factor of 10 (see footnote f to Table 1). There are 18 such substances in rats and 12 in mice. For these carcinogens, any summary measure of

Table 2. Ratio of harmonic, geometric, and arithmetic means to most potent TD_{50} for chemicals positive in more than one experiment, by species.

Ratio of mean TD_{50} to most potent	Rats N=163			Mice N=176		
	H	G	A	H	G	A
	%	%	%	%	%	%
1-1.99	88	74	61	92	78	72
2-2.99	9	15	19	7	14	12
3-3.99	2	3	7	0	7	6
4-9.99	1	6	9	1	1	8
≥ 10	0	2 ^a	4 ^a	0	0	2 ^a
Total	100%	100%	100%	100%	100%	100%

Legend:

H = Ratio of harmonic mean (T_H) to most potent TD_{50} (T_P)

G = Ratio of geometric mean (T_G) to most potent TD_{50} (T_P)

A = Ratio of arithmetic mean (T_A) to most potent TD_{50} (T_P)

^aChemicals with values of ratio greater than 10. Those followed by “*” were in the extreme category for both arithmetic and geometric means.

Rats:

AF-2; Aflatoxin B1; Aniline.HCl; Nitrosomethylaniline (*);

Sodium Saccharin; TCDD (*); Vinyl Chloride (*)

Mice:

Benzene; 4-Chloro-o-Toluidine.HCl; Phenacetin

potency masks the variation across experiments. While noting that the number of such cases is small, we have investigated possible reasons for these widely differing potency estimates for a chemical within a species. We first compared the frequency of estimates varying more than 10-fold to the frequency observed for near-replicate experiments (Table 3). In an earlier paper (6), we examined reproducibility of results in 66 comparisons consisting of 2 or more bioassays of the same chemical administered by the same route and using the same sex and strain of rat or mouse. Here we update this analysis to include 35 additional comparisons from our more recent plots of the CPDB (5,6). Overall, there was good reproducibility of positivity; among the 101 comparisons, 51 were concordant and positive in all of the near-replicate tests, 35 were concordant and negative, and 15 were discordant. For each species, we took the ratio of the least potent TD_{50} and the most potent TD_{50} in each concordant-positive near-replicate case, and we compared the distribution of these ratios to the distribution of all chemicals having more than one positive experiment, i.e., those chemicals reported in Table 2. (The chemicals with near-replicate tests are also included in the larger distribution, but the TD_{50} values for those substances may be from different experiments.) Table 3 indicates that the distribution of the ratio of least to most potent TD_{50} values for all chemicals is similar to that for the near-replicate comparisons. This similarity suggests that the discrepant results for a chemical within a species are not an artifact of combining across strains, routes of administration, and sexes.

We also compared the extreme cases (TD_{50} values discrepant by > 10-fold) to all other chemicals in Table 1 with more than one positive experiment, in terms of how often they were tested. In mice, 92% of the extreme cases were tested more than twice compared to 33% of all other cases; in rats, 89% of extremes were tested more than twice compared to 42% of others. There are similar differences in the number of positive tests for the two groups. Thus, when there are extreme differences between TD_{50} values from different tests of the same chemical, the selection of the least and most potent

Table 3. Ratio of least to most potent TD_{50} from different positive experiments for near-replicate comparisons and all chemicals with more than one positive experiment, by species.

Ratio of least potent TD_{50} to most potent	Rats		Mice	
	Near-replicate tests	All chemicals	Near-replicate tests	All chemicals
	N (%)	N (%)	N (%)	N (%)
1-1.99	15 (55)	76 (46)	13 (54)	90 (51)
2-2.99	4 (15)	21 (13)	6 (25)	35 (20)
3-3.99	3 (11)	19 (12)	0 (0)	11 (6)
4-9.99	2 (8)	29 (18)	4 (17)	28 (16)
≥ 10	3 (11)	18 (11)	1 (4)	12 (7)
Total	27 (100)	163 (100)	24 (100)	176 (100)

values was made from among a larger number of TD₅₀ values.

Finally, we investigated whether differences between the dose levels administered in the comparison tests were greater for the extreme cases. Generally, within a species the doses in different tests of the same chemical are quite similar. We computed the ratio of maximum doses tested in the experiments that yielded the minimum and maximum TD₅₀ values. The median of this ratio for the cases that were not extreme (i.e., differed by less than a factor of 10) was 1.09 for mice and 1.25 for rats. We found that three-quarters of the extreme cases with a ratio > 10 were above this median in each species. This result is not surprising since generally the TD₅₀ value is restricted by the maximum dose tested in a bioassay, i.e., a statistically significant TD₅₀ cannot be very far from the administered dose, given the usual experimental design (13).

We thank Bruce N. Ames for his continued advice, Kenneth Brown for his early contributions to this work, and Michael Dunker for technical support. This work was supported by NIEHS/DOE Interagency Agreement 222-Y01-ES-10066 through the Lawrence Berkeley Laboratory.

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